

Diagnostic companies developing KRAS tests likely to see first impact of comparative effectiveness, industry experts say

by Elizabeth Krutholow and Kimberly Ha

Diagnostic companies developing KRAS tests are likely the first to be impacted by comparative effectiveness studies, industry experts said.

Quest Diagnostics (NYSE:DGX), LabCorp (NYSE:LH), DxS and Genomic Health (NASDAQ:GHDX) are some companies developing KRAS tests.

The FDA Oncologic Drugs Advisory Committee (ODAC) panel discussion last December debated whether retrospective studies could be used to demonstrate that KRAS is a reliable biomarker to predict response to EGFR drugs, such as Erbitux or Vectibix.

Comparative effectiveness research refers to the comparison of different types of treatments for the same disease. In many countries, cost is also taken into account. A KRAS diagnostic will help predict which patients with colorectal cancer are likely to respond to EGFR drugs.

Both the American Society of Clinical Oncology (ASCO) and NCCN have updated their guidelines to say KRAS testing should be integrated into clinical practice to determine which patients should be treated with these drugs in colorectal cancer.

"Based on the ASCO recommendations, a key place that we should immediately target and implement comparative effectiveness is KRAS [testing]," said Kenneth H. Buetow, Ph.D, associate director responsible for bioinformatics and information technology at the National Cancer Institute.

KRAS diagnostics are one area that will see expansion, Buetow added.

David Blumberg, advisory sector leader for pharmaceuticals at KPMG, noted that there is increasing recognition that a drug that might be the right therapy on average may not be the right choice for specific patient subgroups.

Personalized medicine research will likely expand in areas such as cancer, cardiovascular disease and neurosciences, and the companion diagnostics that go with therapeutics in these indications, noted Paul Keckley, PhD, executive director of Deloitte Center for Health Solutions.

The question remains how personalized therapeutics and companion diagnostics will be incorporated within comparative effectiveness, experts said.

"Comparative effectiveness will affect diagnostic companies," said Edward Abrahams, Ph.D., executive director of the Personalized Medicine Coalition. His non-profit organization is working on legislative language to integrate the principles of personalized medicine in comparative research efforts, to improve clinical outcomes and reduce costs.

A focus on cost effectiveness would be beneficial for diagnostic companies, said Bruce Quinn, senior health policy specialist at Foley Hoag. Especially if the drug is expensive, the cost savings of personalizing treatment will have a total impact on society, and a return on investment, he said. Language in the stimulus bill, however, prevents any comparative effectiveness research from looking at cost as a factor. Most experts believe that cost will eventually be used.

The cost of treating metastatic colorectal cancer could be cut by as much as USD 604m a year, if all patients were tested for KRAS mutation status, according to a study last year by Dr Veena Shankaran of Northwestern

University in Chicago.

Payors and insurers want clear evidence that the test will improve cost effectiveness, especially if the diagnostic is linked to a therapy, Quinn said.

Under comparative effectiveness, diagnostics matter only if they change the clinical management of patients, said Dr Mark Charny, founder of Translucency, a consultancy firm specializing in reimbursement strategies across the EU. If the ultimate outcome is the same, with or without the test, the diagnostic is useless, he said.

"There is implicit comparative effectiveness with KRAS," Charny said.

Reimbursement for diagnostics will depend on the predictive value of the test, and payors will take into account whether it disrupts the course of care, or introduces a new intervention, added Keckley.

National plans, such as UnitedHealth, Cigna and Blue Cross, will cover these diagnostics under very precise inclusion criteria, Keckley said. That tends to be the way things are introduced into the US system, he added.

According to a Blue Cross executive summary on KRAS testing, the technology must have final approval from appropriate regulatory bodies, must improve the net health outcome and be as beneficial as any established alternatives. In addition, the improvement in testing must be attainable outside the investigational settings and the scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

Companies like Quest Diagnostics and LabCorp hide behind independent labs and beat everyone in volume, thereby receiving the greatest benefit from the Medicare fee schedule, said a health policy consultant on background.

Yet drugs like Erbitux and Vectibix have not been relabeled for use with KRAS testing.

Thomas Li, chief technology officer at Roche Molecular Diagnostics, said when the test is not in the label, insurance companies can be reluctant to pay for it. "They're always reluctant to pay for new things. If it's not in the label, it gives them an excuse," he said.

However, diagnostics developed for marketed drugs are not held to the same standards as diagnostics that are co-developed with the therapeutic, Quinn said. Even if a drug is labeled for use with a particular companion diagnostic, other tests can be reimbursed, he said. There are several public insurance companies that are currently covering KRAS testing, Quinn noted.

For molecularly informed comparative effectiveness, the appropriate incentives model has to be created, said Buetow. The FDA is very interested in molecular diagnostics, and is actively pursuing what should be done, he said.

"You can't have one without the other. You won't improve quality and reduce costs, unless the principles of personalized medicine are there," Abrahams said.